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Commentary

Effectiveness of Ivermectin in Treatment of COVID-19 Patients

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DESCRIPTION

Ivermectin is a Food and Drug Administration (FDA) approved anti-parasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiases, and scabies. It's also being estimated for its capability to reduce the rate of malaria transmission by killing mosquitoes that feed on treated humans and livestock. For these suggestions, ivermectin has been extensively used and is generally well permitted. Ivermectin isn't approved by the FDA for the treatment of any viral infection.

Reports from *in vitro* studies suggest that ivermectin acts by inhibiting the host importing alpha/ beta-1 nuclear transport proteins, which are part of a crucial intracellular transport process that viruses hijack to enhance infection by suppressing the host's antiviral response. In addition, ivermectin docking may interfere with the attachment of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein to the human cell membrane. Ivermectin is thought to be a host- directed agent, which may be the basis for its broad- spectrum activity *in vitro* against the viruses that cause dengue, Zika, HIV, and yellow fever. Despite this in vitro activity, no clinical trials have reported a clinical benefit for ivermectin in patients with these viruses. Some studies of ivermectin have also reported implicit anti-inflammatory properties, which have been supposed to be advantageous in people with COVID-19.

Ivermectin has been shown to inhibit the replication of SARS-CoV-2 in cell cultures. Still, pharmacokinetic and pharmacodynamic studies suggest that achieving the plasma concentrations necessary for the antiviral efficacy detected *in vitro* would require administration of doses up to100-fold higher than those approved for use in humans. Indeed though ivermectin appears to accumulate in the lung tissue, predicted systemic plasma and lung tissue concentrations are much lower than 2 μM, the half-maximal inhibitory concentration (IC50) against SARS-CoV-2 *in vitro*. Subcutaneous administration of ivermectin 400 μg/ kg had no effect on SARS-CoV-2 viral loads in hamsters. Still, there was a reduction in olfactory deficiency (measured using a food- finding test) and a reduction in the interleukin (IL)-6 IL-10 ratio in lung tissues.

Since the last modification of this section of the Guidelines, the results of several randomized trials and retrospective cohort studies of ivermectin use in patients with COVID-19 have been published in peer- reviewed journals or have been made available as scripts ahead of peer review. Some clinical studies showed no benefits or worsening of disorder after ivermectin use, whereas others reported shorter time to resolution of disorder manifestations that were attributed to COVID-19, greater reduction in inflammatory marker levels, shorter time to viral clearance, or lower mortality rates in patients who took ivermectin than in patients who took comparator medicines or placebo.

Still, utmost of these studies had deficient information and significant methodological limitations, which make it tough to eliminate common causes of bias. These limitations include The sample size of utmost of the trials was small, varied doses and schedules of ivermectin were used, some of the randomized controlled trials were open- label studies in which neither the participants nor the investigators were blinded to the treatment arms, patients took various concomitant drugs (e.g.,doxycycline, hydroxychloroquine, azithromycin, zinc, corticosteroids) in addition to ivermectin or the comparator medicine. This confounded the assessment of the efficacy or safety of ivermectin, the severity of COVID-19 in the study participants wasn't always well described, the study outcome measures weren't always easily defined.

In animal studies, ivermectin was shown to be teratogenic when given in doses that were maternotoxic. These results raise concerns about administering ivermectin to people who are in the early stages of pregnancy (previous to 10 weeks gestation). A 2020 methodical review and meta- analysis reviewed the prevalence of poor maternal and fetal outcomes after ivermectin was used for its anti-parasitic properties during pregnancy. Still, the study was unable to establish a causal relationship between ivermectin use and poor maternal or fetal outcomes due to the quality of evidence. There are numerous reports of inadvertent ivermectin use in early pregnancy without apparent adverse effects. Therefore, there's deficient confirmation to establish the safety of using ivermectin in pregnant people, especially those in the later stages of pregnancy. One study reported that the ivermectin concentrations secreted in breast milk after a single oral dose were relatively low. No studies have estimated the ivermectin attention in breast milk in patients who took multiple doses.

Several clinical trials that are assessing the use of ivermectin for the treatment of COVID-19 are presently underway or in development.

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